Original Article

Using kidney size for early detection of contrast-induced nephropathy in the emergency department setting

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Aim: We aimed to examine the relationship between kidney size and contrast-induced nephropathy (CIN) in patients who underwent contrast-enhanced computed tomography (CT) in the emergency department.

Methods: This single-center retrospective observational study was undertaken to evaluate risk factors for CIN at Okayama Saiseikai General Hospital (Okayama, Japan) from January 2014 through to December 2016. Contrast-induced nephropathy was defined as an absolute increase in serum creatinine level of ≥ 0.5 mg/dL or $\geq 25\%$ over the baseline value within 72 h after contrast-enhanced CT. Independent risk factors for CIN were determined by multiple logistic regression analysis. The thickness of the kidney was evaluated as a predictor of CIN using the area under the receiver operating characteristic curve. We also analyzed CIN as an outcome using the Kaplan–Meier method.

Results: The incidence of CIN was 26/262 (9.9%). In the multivariate analysis, CIN was associated with renal thickness (odds ratio = 0.65; 95% confidence interval, 0.53–0.81). No patient underwent renal replacement therapy.

Conclusion: Renal thickness could be used as a reliable, simple, and easily obtainable marker for identifying CIN in patients undergoing contrast-enhanced CT in the emergency department.

Key words: Contrast-induced nephropathy, emergency department, kidney size, renal thickness

INTRODUCTION

CONTRAST -enhanced computed tomography (CT) is used to assist diagnosis and therapy selection in the emergency department (ED). Anaphylaxis and contrast-induced nephropathy (CIN) are widely recognized as common adverse effects of contrast media. Some studies have reported an incidence of CIN as high as 11% and have linked CIN to a twofold increased risk of major adverse events within 1 year.[1] Risk factors for CIN include the estimated glomerular filtration rate (eGFR), age, sex, anemia, chronic heart failure, and some medications. In particular, patients with chronic kidney disease (CKD) may be at risk of CIN.[2–4] The eGFR is an essential diagnostic tool for CKD.[5] However, some patients are hemodynamically unstable, or in the state of sarcopenia or frailty at the ED. In some cases, serum creatinine (sCr) concentration and eGFR do not accurately reflect renal function because creatinine-based GFR estimation is greatly influenced by physiological and clinical conditions that affect body muscle mass.[6] Additionally, in severe life-threatening conditions, we often need to undertake contrast-enhanced CT without laboratory findings. Therefore, CT-based markers need to be identified to estimate renal function rapidly.

According to published reports, kidney size is related to renal function.[7] If it were possible to evaluate the risk of CIN based on kidney size alone, then this would provide a simple and easy method of CIN risk assessment. Therefore, we investigated whether the thickness of the kidney is a risk factor for CIN in patients who undergo contrast-enhanced CT.

MATERIALS AND METHODS

Ethics statement

THE STUDY PROTOCOL for this research project was approved by a suitably constituted Ethics Committee of

the institution, and it conforms to the provisions of the Declaration of Helsinki (Committee of Okayama Saiseikai General Hospital, Okayama, Japan). Informed consent was obtained from all patients.

Study design

We carried out a retrospective cohort study of outpatients who underwent contrast-enhanced CT imaging after administration of i.v. contrast media from January 2014 through to December 2016 at the ED of Okayama Saiseikai General Hospital. Radiographers determined the types and doses of contrast media. We used a multidetector-row CT scanner (Aquilion Prime; Toshiba Medical Systems, Tochigi Prefecture, Japan). Only non-ionic low osmolar contrast media were given to all patients in the study. The study exclusion criteria included age <15 years, ongoing dialysis, insufficient laboratory data, and discharge within 72 h.

Data collection

We collected the following data: white blood cell count, hemoglobin, platelet count, blood urea nitrogen, sCr, eGFR values (calculated using the Modification of Diet in Renal Disease method), total protein, albumin, C-reactive protein, clinical information (age, sex, weight, height, and body mass index), prognostic nutritional index, contrast media dose, medical history (diabetes, hypertension, cerebrovascular disease, congestive heart failure, CKD, and cancer), previous use of medications (such as stains, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, and diuretics), and total psoas area (the sum of the average cross-sectional area of each psoas muscle) at the L3 level,[8] shock vitals on admission, and the indication for the contrast-enhanced CT. We also analyzed the time to recovery to the Cr value on admission.

Method of measurement

The method of measurement is depicted in Figure 1. The kidney size was measured manually using the distances between CT images. We measured the kidney on the slice surface of the renal vein. Linear renal dimensions (depth, width, length, and thickness) were measured. Renal depth was measured as the distance from the renal hilum to the opposite side on the axial view. Renal width was measured as the longest distance on an axis perpendicular to the renal width on the axial view. Renal length was measured as the pole-to-pole distance on the coronal view of the CT image with a 5-mm slice. Renal thickness was measured as the longest straight distance from the renal calyx to renal the

surface. We took measurements of both the right and left kidneys and calculated their mean values. Renal volume was calculated in cubic centimeters using the following formula:[9,10] renal volume (cm^3) = length × width × depth × π/6.

Definitions

Contrast-induced nephropathy was defined as an absolute increase in the sCr level of ≥0.5 mg/dL or ≥25% over the baseline value within 72 h after contrast-enhanced CT.[2,11] Acute kidney injury was defined according to the Acute Kidney Injury Network/Kidney Disease: Improving Global Outcomes guidelines: stage 1, absolute increase in sCr level ≥0.3 mg/dL or a 1.5–1.9-fold increase over the baseline sCr level; stage 2, 2.0–2.9-fold increase over the baseline sCr level; and stage 3, 3.0-fold increase over the baseline sCr level, increase in sCr level ≥4.0 mg/dL, or initiation of dialysis.[11] Acute kidney injury requiring the initiation of renal replacement therapy was defined as stage 3.

Statistical analysis

Continuous variables are presented as median and interquartile range values, whereas categorical variables are shown as frequencies or percentages. Categorical variables were compared using Fisher's exact probability test. The Mann–Whitney *U*-test was used to evaluate variables with non-normal distributions. Receiver operating characteristic (ROC) curve analysis was carried out to assess the diagnostic accuracy of CIN risk factors. Multivariate analysis was carried out using all variables with $P < 0.05$ in the univariate analysis. We also examined the use of renal replacement therapy and analyzed the time taken to recover from CIN using the Kaplan–Meier method. Using Pearson's correlation analysis, we analyzed the relationship between kidney thickness and kidney volume. A value of $P < 0.05$ was considered statistically significant. All statistical analyses were undertaken using EZR version 1.11 (Jichi Medical University, Shimotsuke, Japan).

RESULTS

Study cohort characteristics

DURING THE 3 -year study period, a total of 314 patients were admitted to the ED of our hospital to undergo contrast-enhanced CT by emergency physicians. Of these patients, 262 met the inclusion criteria. Figure 2 shows the derivation of the study population and workup for CIN. Among the 262 patients, the incidence of CIN was 26 (9.9%). The demographic and clinical characteristics of the
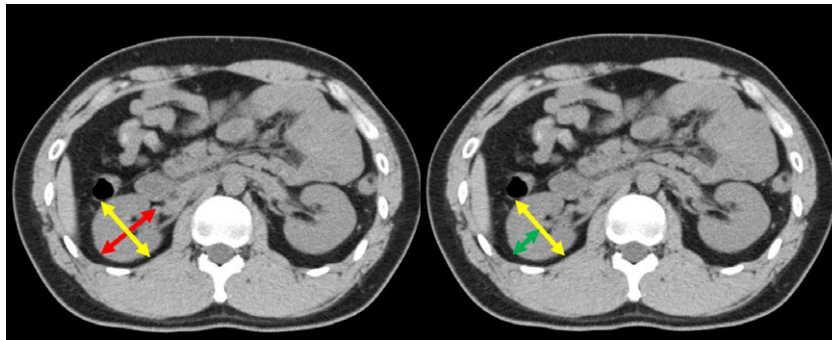
Fig. 1. Kidney size was measured manually in patients who underwent contrast-enhanced computed tomography in the emergency department, using the distance between computed tomography images in the slice of the renal vein. Renal depth (red arrows) was measured as the distance from the renal hilum to the opposite side on the transverse plane. Renal width (left panel, yellow arrow) was measured as the longest distance on an axis perpendicular to the renal width on the transverse plane. Renal thickness (right panel, green arrows) was measured as the straight distance from the renal calyx to the opposite side on the transverse plane.
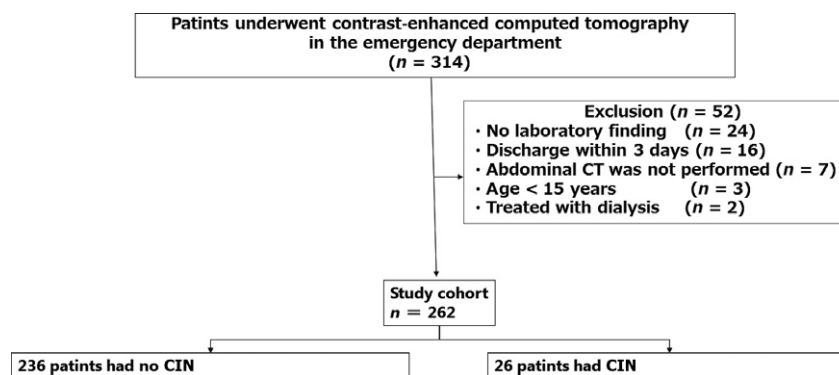
Fig. 2. Flowcharts of patients with contrast-induced nephropathy (CIN) or no CIN who underwent contrast-enhanced computed tomography in the emergency department.

cohort are shown in Table 1. There was no significant difference in demographic characteristics between the patients with and without CIN.

Risk factors for CIN

According to the multiple logistic regression analysis, CIN occurrence was only significantly associated with renal thickness (odds ratio = 0.65; 95% confidence interval, 0.53–0.81; Table 2).

Renal thickness for CIN screening

In the ROC analysis of CIN (Fig. 3), the cut-off value for renal thickness that optimally predicted CIN was found to be approximately 18.3 mm. We selected the cut-off value that maximized the sum of sensitivity and specificity. At the cut-off, the sensitivity and specificity for predicting CIN were 79%

and 65%, respectively. The area under the ROC curve for renal thickness was 0.79 (95% confidence interval, 0.70–0.88).

Outcomes of CIN

Figure 4 shows the 90-day outcomes of CIN cases. No patient required renal replacement therapy.

Correlation between kidney volume and kidney thickness

The correlation coefficient between kidney volume and kidney thickness was 0.56 ($P < 0.05$).

DISCUSSION

T O THE BEST of our knowledge, this is the first study to investigate the incidence of CIN that has focused on

Table 1. Characteristics of patients who underwent contrast-enhanced computed tomography in the emergency department (*n* = 262)

	CIN negative (*n* = 236)	CIN positive (*n* = 26)	*P*-value
Male gender, *n*	142/236	14/26	0.536
Age, years	71 (61–81)†	73.5 (60–83.5)†	0.350
Height, cm	160 (152–166)†	162.5 (150–165)†	0.828
Weight, kg	52.0 (44.1–61.6)†	52.3 (47.3–71.8)†	0.259
Body mass index	20.6 (18.6–23.6)†	23.2 (19.1–25.1)†	0.144
Prognostic nutritional index	43.8 (37.3–49.7)†	44.23 (38.4–50.6)†	0.566
Nephrotoxic drugs, *n*	114/236	18/26	0.061
Hypertension, *n*	86/236	15/26	0.054
Diabetes, *n*	37/236	5/26	0.582
CVD, *n*	35/236	5/26	0.566
CHF, *n*	58/236	10/26	0.156
Cancer, *n*	55/236	2/26	0.080
CKD, *n*	78/236	8/26	1.000
Purpose of contrast-enhanced CT			
Gastrointestinal disease, *n*	162/236	16/26	0.509
Cardiovascular disease, *n*	13/236	2/26	0.650
Lung disease, *n*	8/236	2/26	0.260
Brain disease, *n*	12/236	3/26	0.176
Infection, *n*	10/236	2/26	0.338
Trauma, *n*	23/236	1/26	0.485
Others, *n*	8/236	0/26	1.000
Dose of contrast medium, mL	100 (100–135)†	100 (100–100)†	0.314
Total protein, g/dL	6.7 (6.1–7.1)†	6.6 (6.3–6.9)†	0.893
Albumin, g/dL	3.7 (3.2–4.2)†	3.6 (3.1–4.2)†	0.695
White blood cells, μL	9,735 (6,912–12,527)†	9,695 (8,570–13,422)†	0.433
Hemoglobin, g/dL	12.2 (10.4–13.9)†	12.9 (11.0–13.8)†	0.414
Platelets, 10^4/μL	20.8 (15.9–25.9)†	21.1 (15.9–26.3)†	0.860
C-reactive protein test, mg/dL	0.76 (0.08–5.74)†	0.78 (0.15–6.66)†	0.874
BUN, mg/dL	16.8 (12.6–22.2)†	16.5 (11.9–22.4)†	0.764
Serum creatinine, mg/dL	0.74 (0.60–0.93)†	0.69 (0.52–0.84)†	0.208
eGFR, mL/min	71.5 (59.0–88.7)†	77.7 (57.5–99.7)†	0.409
Creatinine clearance, mL/min	36.7 (24.6–53.5)†	35.4 (25.4–49.2)†	0.690
Shock vitals on admission	18/236	2/26	1.000
Depth, cm	4.95 (4.63–5.54)†	4.79 (4.27–5.09)†	0.020
Width, cm	4.79 (4.46–5.19)†	4.98 (4.16–5.19)†	0.393
Length, cm	10.7 (10.0–11.2)†	10.2 (9.75–10.50)†	0.007
Thickness, cm	2.03 (1.86–2.23)†	1.75 (1.56–1.91)†	<0.001
Renal volume, cm^3	130.1 (115.2–152.4)†	125.8 (100.5–144.2)†	0.045
TPA, cm^2/m^2	3.45 (2.77–4.13)†	2.60 (2.04–3.69)†	0.009
KDIGO			
Stage 1	0/236	23/26	
Stage 2	0/236	3/26	
Stage 3	0/236	0/26	

†Continuous variables are presented as median and interquartile range values. Categorical variables are shown as frequencies or percentages. *P*-values were calculated using Fisher's exact probability test or Mann–Whitney *U*-test. Acute kidney injury was defined according to the Acute Kidney Injury Network/Kidney Disease: Improving Global Outcomes (KDIGO) guidelines: stage 1, absolute increase in serum creatinine (sCr) level ≥0.3 mg/dL or a 1.5–1.9-fold increase over the baseline sCr level; stage 2, 2.0–2.9-fold increase over the baseline sCr level; and stage 3, 3.0-fold increase over the baseline sCr level, increase in sCr level ≥4.0 mg/dL, or initiation of dialysis.
BUN, blood urea nitrogen; CIN, contrast-induced nephropathy; CHF, congestive heart failure; CKD, chronic kidney disease; CVD, cerebrovascular disease; eGFR, estimated glomerular filtration rate; TPA, average of the cross-sectional area of each psoas muscle.

kidney size. There were three major findings. First, our study showed a 9.9% incidence of CIN among patients undergoing contrast-enhanced CT in the ED. This finding is similar to a previous report by Fukushima *et al.*,[12] who found that the overall incidence of CIN was 5.1% in a study of 216 patients who underwent contrast-enhanced CT examination. Second, the results of our study showed that renal thickness was easily obtained and significantly associated with CIN. In the multivariate logistic regression analysis, renal thickness was found to be independently associated with CIN. Finally, the renal function prognosis of CIN was favorable.

The diagnosis of CIN depends on the sCr level.[11] The sCr or eGFR level has historically been chosen as the standard parameter for renal function. In fact, current guidelines for

Table 2. Multiple logistic regression analysis of risk factors for contrast-induced nephropathy

Risk factor	Multivariate analysis		
	OR	95% CI	*P*-value
TPA	1.00	0.98–1.02	0.988
Renal volume	0.88	0.59–1.32	0.553
Renal thickness	0.65	0.53–0.81	<0.001

CI, confidence interval; OR, odds ratio; TPA, average of the cross-sectional area of each psoas muscle.

CIN indicate sCr or eGFR levels might indicate an increased risk of CIN. However, sCr and eGFR levels might not accurately reflect renal function. Both sCr and eGFR levels are greatly influenced by physiological and clinical conditions that affect body muscle mass.[6] The sCr levels of sarcopenic elderly persons are usually low or below normal ranges.[13] In contrast, patients in a state of acute kidney injury usually have sCr levels that are high or exceed normal ranges.[14] More generally, the hemodynamic states and characteristics of patients are especially liable to change with time in the ED setting. The sCr and eGFR levels might not reflect renal function accurately in EDs. In our study, sarcopenia might have affected eGFR estimation.
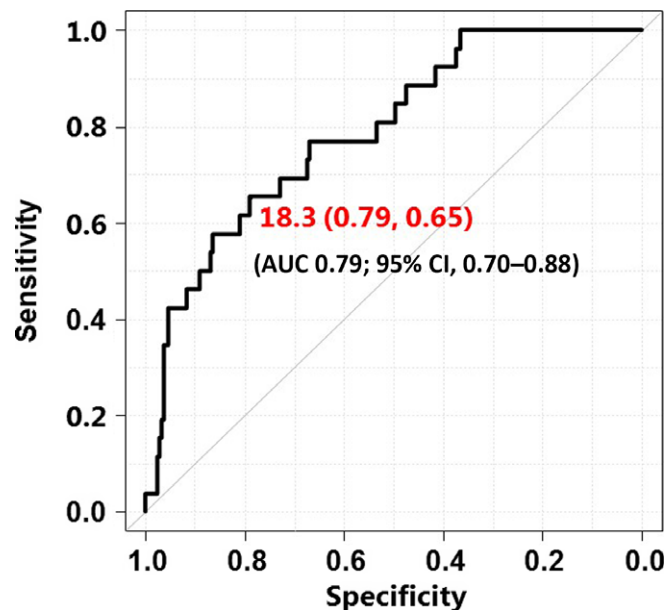
Our study also showed favorable outcomes of CIN. No patient required renal replacement therapy. This result is consistent with previous studies.[15] The time required for complete recovery from CIN could range from at least days to weeks.[11] Another study has suggested that use of contrast media was not associated with increased frequency of acute kidney injury.[16]

This study showed that renal thickness is an easily obtained and significant marker of CIN. Gupta *et al.*[7] previously investigated the relationship between renal function and renal volume. They used 3-D CT to delineate renal parenchyma on each contiguous axial section covering the entire kidney. Breau *et al.*[9] suggested that 2-D CT provides a simple approach to measuring renal volume. However, all


Fig. 3. Receiver operating characteristic curves of renal thickness in 262 patients who underwent contrast-enhanced computed tomography in the emergency department. The cut-off value for renal thickness was 1.83 cm, at which the sensitivity and specificity were 79% and 65%, respectively. The area under the curve for renal thickness was 0.79 (95% confidence interval, 0.701–0.877).
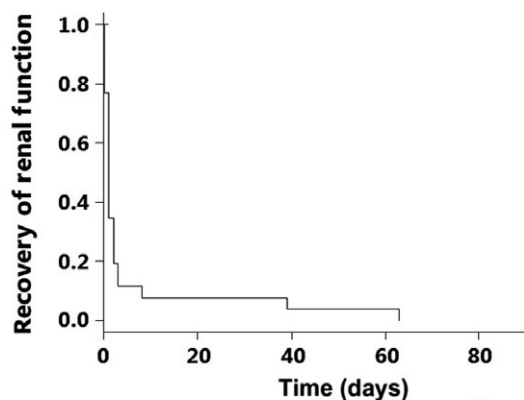
Fig. 4. Ninety-day survival curve for renal function in patients who underwent contrast-enhanced computed tomography in the emergency department and developed contrast-induced nephropathy. All patients recovered baseline renal function. No patient needed renal replacement therapy.

evaluations of kidney volume are impractical in the ED because they waste additional time. Our study suggests that kidney thickness is correlated with kidney volume ($r = 0.56$, $P < 0.05$). Multivariate analysis showed no significant differences in kidney volume; however, kidney volume and thickness might be related. Some studies have reported early predictors for acute kidney injury, such as serum cystatin C, kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, interleukin-18, liver fatty acid binding protein, tissue inhibitor of metalloproteinases-2, and insulin-like growth factor-binding protein 7 as urinary biomarkers.[17–19] These are probably accurate biomarkers for estimating patient status. However, they remain under study, and money and time are required to obtain evaluation results. By comparison, renal thickness is a simple and easily obtainable marker for estimating renal function. This parameter for the detection of CIN is useful in severe life-threatening conditions that require the use of i.v. contrast media for contrast-enhanced CT imaging without laboratory findings, and in patients with sarcopenia. Saline solution should be administered to prevent CIN in patients with reduced kidney thickness.

This study has several limitations. First, it has a single-center retrospective observational design. The number of patients entered into the analysis was small. A multicenter study with a prospective design might be desirable in the future. However, obtaining consent from patients and family members may be difficult for such a study, and it would be ethically questionable. Second, kidney size is influenced by various factors including age, sex, height, weight, right or left side, the presence of acute kidney injury, and diabetes.[7]

Toda *et al.*[20] investigated the efficiency of tolvaptan focusing on kidney size. The kidney sizes of responders to tolvaptan were longer than those of non-responders. In our study, the kidney thickness among patients without CIN was 2.03 cm (1.89–2.23 cm), whereas the kidney thickness among those with CIN was 1.75 cm (1.56–1.91 cm). Their kidneys were slightly atrophic. It has been reported that kidney size is correlated with renal function.[20] Third, the accumulated cohort could have been subject to selection bias, especially in cases with severe laboratory results for sCr or eGFR. The decision to carry out contrast-enhanced CT is determined by the individual emergency physician, and most clinicians would not prescribe contrast agents to high-risk patients such as the elderly and those with eGFR <45 mL/min/1.73 m^2.[2] However, we undertook contrast-enhanced CT on all patients who required hospitalization, such as those with generalized peritonitis, trauma, and pulmonary embolism. No patient underwent another contrast-enhanced CT after admission. Finally, we were not able to record the volumes of fluid replacement accurately. However, we only gave crystalloid fluids. Further research might be needed to confirm the efficiency of kidney size as an indicator of patients who are at high risk for CIN and who need treatment.

CONCLUSION

IN THIS RETROSPECTIVE analysis carried out at our ED, we found that the thickness of the kidney was a risk factor for CIN. In cases of CIN, the likelihood of kidney recovery is favorable.

DISCLOSURE

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